

CLAIMS

1. A pharmaceutical composition comprising a mixture of :
  - 5 (a) an active macromolecular principle, and
  - (b) an aromatic alcohol absorption enhancer chosen from butylated hydroxy toluene, butylated hydroxy anisole and analogues and derivatives thereof, wherein the aromatic alcohol absorption enhancer is present in an amount by weight greater than or equal to that of the active macromolecular principle.
- 10 2. A pharmaceutical composition comprising a mixture of :
  - (a) an active macromolecular principle,
  - (b) an aromatic alcohol absorption enhancer chosen from propyl gallate, butylated hydroxy toluene, butylated hydroxy anisole and analogues and derivatives thereof, wherein the aromatic alcohol absorption enhancer is present in an amount by
  - 15 weight greater than or equal to that of the active macromolecular principle, and
  - (c) a solubilisation aid capable of increasing the solubility of the aromatic alcohol absorption enhancer in aqueous media.
3. A composition according to claim 1 or 2, wherein the mixture comprises less than 5% by weight of water.
- 20 4. A composition according to any of claims 1 to 3, wherein the composition is coated with an enteric coating which becomes permeable at a pH of from 3 to 7.
5. A composition according to any preceding claim, wherein the mixture comprises at least 1% by weight of the aromatic alcohol absorption enhancer.
- 25 6. A composition according to any preceding claim, wherein the ratio by weight of the aromatic alcohol absorption enhancer to active macromolecular principle is at least 5:1.
7. A composition according to any preceding claim, wherein the mixture is in the form of a solution or a microparticulate dispersion.
- 30 8. A composition according to any preceding claim, wherein the mixture is in solid form.
9. A composition according to any preceding claim, wherein the active macromolecular principle is a polypeptide or protein, polynucleotide, polysaccharide or a mixture thereof.
- 35 10. A composition according to any preceding claim, wherein the aromatic alcohol absorption enhancer is chosen from BHT, BHA and analogues and

derivatives thereof, including analogues and derivatives of hydroxy toluene or hydroxy anisole where the methyl group or the methoxy group linked to the aromatic ring and/or the hydrogen ortho to the hydroxyl group are replaced by linear or branched chain C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkyloxy, C<sub>1-12</sub> alkylthio or C<sub>2-12</sub> alkenyl, either  
5 unsubstituted or substituted in any position, especially by halogen atoms.

11. A composition according to any one of claims 2 to 9, wherein the aromatic alcohol absorption enhancer is propyl gallate or an analogue or a derivative thereof, including esters of gallic acid, where the esters may be linear or branched chain C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkyloxy, C<sub>1-12</sub> alkylthio or C<sub>2-12</sub> alkenyl esters, and the  
10 compounds are optionally substituted with halogen, linear or branched chain C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkyloxy, C<sub>1-12</sub> alkylthio or C<sub>2-12</sub> alkenyl esters.

12. A composition according to any of claims 2 to 11, where the solubilisation aid is chosen from a bile acid or salt, benzyl alcohol, phenyl ethanol, phenoxyethanol, transcitol and isopropanol.

13. A composition according to any preceding claim, where the active  
15 macromolecular principle is insulin, calcitonin, growth hormone, parathyroid hormone, or erythropoietin, and derivatives and analogues, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.

14. A composition according to any preceding claim, where the active  
20 macromolecular principle is insulin, calcitonin, parathyroid hormone or a derivative or an analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.

15. A composition according to claim 14, where the active  
25 macromolecular principle is insulin or a derivative or an analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin and the composition further comprises an insulin sensitizing agent.

16. A composition according to any preceding claim, for use in the therapeutic or diagnostic treatment of the human or animal body.

17. Use, in a pharmaceutical composition, of an aromatic alcohol chosen  
30 from butylated hydroxy toluene, butylated hydroxy anisole and analogues and derivatives thereof as an enhancer for the absorption of a macromolecule across the intestinal wall.

18. Use of an aromatic alcohol chosen from butylated hydroxy toluene,  
35 butylated hydroxy anisole and analogues and derivatives thereof in the manufacture

of a medicament containing an active macromolecular principle, in order to enhance absorption of the active macromolecular principle into the human or animal body.

19. Use, in a pharmaceutical composition, of an aromatic alcohol chosen from propyl gallate, butylated hydroxy toluene, butylated hydroxy anisole and analogues and derivatives thereof together with a solubilisation aid capable of increasing the solubility of the aromatic alcohol absorption enhancer in aqueous media as an enhancer for the absorption of macromolecules across the intestinal wall.

20. Use of an aromatic alcohol chosen from propyl gallate, butylated hydroxy toluene, butylated hydroxy anisole and analogues and derivatives thereof together with a solubilisation aid capable of increasing the solubility of the aromatic alcohol absorption enhancer in aqueous media in the manufacture of a medicament containing an active macromolecular principle, in order to enhance absorption of the active macromolecular principle into the human or animal body.

21. Use according to any one of claims 17 to 20, wherein the composition comprises less than 5% by weight of water.

22. Use according to any of claims 19 or 20, wherein the solubilisation aid is chosen from a conjugated bile acid or salt, benzylalcohol, phenylethanol, phenoxyethanol, transcitol and isopropanol.

23. Use according to any of claims 18 or 20, wherein the medicament is provided in the form of a solution, as a microparticulate dispersion or as a solid.

24. Use according to any of claims 17 to 23, wherein the macromolecule to be absorbed/active macromolecular principle is a polypeptide or protein, polynucleotide, polysaccharide or a mixture thereof.

25. Use according to claim 24, wherein the macromolecule to be absorbed/active macromolecular principle to be absorbed is chosen from insulin, calcitonin, growth hormone, parathyroid hormone and erythropoietin, and derivatives and analogues thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.

26. Use according to claim 25, wherein the macromolecule to be absorbed/active macromolecular principle to be absorbed is insulin, calcitonin, parathyroid hormone or a derivative or an analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.

27. Use according to claim 26, wherein the macromolecular principle is insulin or a derivative or an analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin, and an insulin sensitizing agent is also present.

28. A method of enhancing the absorption of an active macromolecular principle in a patient, which method comprises administering to said patient a composition as defined in any one of claims 1 to 16.

29. A method of treating a patient suffering from a condition or disease  
5 treatable by administration of a composition according to any of claims 1 to 16.